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     FILE 'REGISTRY' ENTERED AT 11:49:24 ON 24 MAR 2009
L1             1 S DOXORUBICIN/CN
L2             1 S PACLITAXEL/CN
L3             1 S CYCLOPHOSPHAMIDE/CN

     FILE 'HCAPLUS' ENTERED AT 11:49:48 ON 24 MAR 2009
L4          1324 S L1 AND L2 AND L3
L5           215 S DOSE-DENSE
L6            19 S L4 AND L5
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

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DICTIONARY FILE UPDATES:  22 MAR 2009  HIGHEST RN 1125392-64-4

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=> s doxorubicin/cn
L1            1 DOXORUBICIN/CN

=> s paclitaxel/cn
L2            1 PACLITAXEL/CN

=> s cyclophosphamide/cn
L3            1 CYCLOPHOSPHAMIDE/CN

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      16.53      16.75

FILE 'HCAPLUS' ENTERED AT 11:49:48 ON 24 MAR 2009
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FILE LAST UPDATED: 23 Mar 2009 (20090323/ED)

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=> s l1 and l2 and l3
         20320 L1
         16784 L2
         18060 L3
L4        1324 L1 AND L2 AND L3

=> s dose-dense
        663778 DOSE
        117794 DENSE
L5         215 DOSE-DENSE
                 (DOSE(W)DENSE)

=> s l4 and l5
L6          19 L4 AND L5

=> d l6 1-19 ti abs bib
```

L6 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Circulating vascular endothelial growth factor, C-reactive protein, and urinary neopterin concentrations during dose-dense chemotherapy

AB Angiogenesis plays a crucial role in tumor progression. Prominent among angiogenic factors is vascular endothelial growth factor (VEGF). VEGF is produced by cancer cells as well as by the cells infiltrating tumor stroma, mainly macrophages. Macrophage activation may be assessed by measuring blood serum or urinary neopterin. Systemic inflammatory response could be evaluated by measuring serum C-reactive protein concns. The aim of the present study was to examine the effect of a regimen combining dose dense combination of doxorubicin and cyclophosphamide with sequential weekly paclitaxel on plasma VEGF, urinary neopterin, and serum C-reactive protein concns. Thirty-four female patients with histol. verified breast carcinoma treated with dose -dense regimen combining doxorubicin and cyclophosphamide with sequential weekly paclitaxel administration were studied. Plasma VEGF was measured by ELISA. Urinary neopterin was determined by high performance liquid chromatog. Compared to baseline plasma VEGF was significantly decreased 1 wk after the start of therapy. VEGF concns. subsequently increased, but this increase was significant compared to baseline only at week 16. Urinary neopterin was significantly increased compared to baseline at every visit with the exception of visits 12 and 20 at which the significance was borderline. Serum C-reactive protein was increased compared to baseline only at visits 4, 6 and 8. A pos. correlation was observed between plasma VEGF and serum C-reactive protein at baseline and at visits 5 and 19. Significant correlations were observed between serum C-reactive protein and urinary neopterin at visits 6, 7, 9, 11, 14, 15, and 17. In conclusion, only minor changes in plasma VEGF and serum C-reactive protein were observed during dose-dense chemotherapy. In contrast, urinary neopterin was increased throughout the course of treatment. Correlations between VEGF and C-reactive protein and

between C-reactive protein and urinary neopterin were observed only at some time points.
AN 2008:1342750 HCAPLUS <<LOGINID::20090324>>
DN 149:505734
TI Circulating vascular endothelial growth factor, C-reactive protein, and urinary neopterin concentrations during dose-dense chemotherapy
AU Melichar, Bohuslav; Ballokova, Anna; Malirova, Eva; Urbanek, Lubor; Krcrnova, Lenka; Hyspler, Radomir; Hornychova, Helena; Ryska, Ales; Solichova, Dagmar
CS Departments of Oncology & Radiotherapy, Charles University School of Pharmacy, Hradec Kralove, Czech Rep.
SO Pteridines (2008), 19(3), 65-71
CODEN: PTRDEO; ISSN: 0933-4807
URL: http://www.pteridines.sk/bild/2008/118/2008-03-01-dose-dense-melichar.pdf
PB International Society of Pteridinology
DT Journal; (online computer file)
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Urinary neopterin, hemoglobin and peripheral blood cell counts in breast carcinoma patients treated with dose-dense chemotherapy
AB Background: Among other actions, chemotherapy may induce an activation of systemic inflammatory and immune response. Patients and Methods: Urinary neopterin was evaluated, using high-performance liquid chromatog., before and during dose-dense combination chemotherapy with doxorubicin, cyclophosphamide and sequential paclitaxel (neoadjuvant or adjuvant) in 194 patients with breast carcinoma. Hb, peripheral blood cell count and, in a subgroup of patients, iron metabolism were also evaluated. Results: Urinary neopterin increased significantly during the chemotherapy. The increase in urinary neopterin was accompanied by a gradual decrease of Hb. A marked increase in serum ferritin concentration was observed during the chemotherapy, along with fluctuations of iron concns. Among 161 patients treated with primary chemotherapy, the pathol. response was evaluable in 150. Pathol. complete response was observed in 37 cases (25%). In patients with pathol. complete response, significantly lower serum ferritin concns. were observed Conclusion: Present data demonstrate the presence of systemic immune activation, reflected in increased urinary neopterin concns., in breast carcinoma patients treated with dose -dense chemotherapy. Lower ferritin concns. were predictive of pathol. complete response.
AN 2008:1037211 HCAPLUS <<LOGINID::20090324>>
DN 150:89895
TI Urinary neopterin, hemoglobin and peripheral blood cell counts in breast carcinoma patients treated with dose-dense chemotherapy
AU Melichar, Bohuslav; Urbanek, Lubor; Krcmova, Lenka; Kalabova, Hana; Melicharova, Karolina; Malirova, Eva; Hornychova, Helena; Ryska, Ales; Hyspler, Radomir; Solichova, Dagmar
CS Department of Oncology & Radiotherapy, Charles University Medical School & Teaching Hospital, Czech Rep.
SO Anticancer Research (2008), 28(4C), 2389-2396
CODEN: ANTRD4; ISSN: 0250-7005
PB International Institute of Anticancer Research
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Dose-dense and/or metronomic schedules of specific chemotherapies consolidate the chemosensitivity of triple-negative breast cancer: a step toward reversing triple-negative paradox
AB A review of recent clin. trials supporting the administration of accelerated chemotherapy schedules (weekly or once every 2 wk) of doxorubicin, cyclophosphamide, and paclitaxel. Once weekly paclitaxel achieves a higher hazard rate reduction than less frequent schedules.
AN 2008:936382 HCAPLUS <<LOGINID::20090324>>
DN 149:416657
TI Dose-dense and/or metronomic schedules of specific chemotherapies consolidate the chemosensitivity of triple-negative breast cancer: a step toward reversing triple-negative paradox
AU Mehta, Rita S.
CS Departments of Division of Hematology/Oncology, Department of Medicine, chao Family Comprehensive Cancer Center, University of California at Irvine School of Medicine, Irvine, CA, USA
SO Journal of Clinical Oncology (2008), 26(19), 3286-3288
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal; General Review
LA English
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI The concept of mathematically optimised dose-scheduling as applied to the adjuvant chemotherapy of primary breast cancer: theory and recent results
AB A review. Theor. analyses and theory-motivated laboratory expts. have confirmed that for anti-mitotic drugs administered by bolus the inter-treatment interval is a critical determinant of ultimate success. Maximum cell kill is best achieved by using the optimal (not necessarily the maximum tolerated) dose level as often as feasible considering the impact of the drug on host toxicity. This approach has been termed 'dose d.', which captures the concept of optimally frequent administration. The feasibility and non-comparative efficacy of the application of this concept was developed in a series of clin. trials at Memorial Sloan-Kettering Cancer Center, New York, USA. These results were used to design an objective, prospectively randomized trial in the Cancer and Leukemia Group B and the North American Breast Intergroup: Study CALGB 9741 involved over 2000 volunteer female patients with node-pos. operable primary breast cancer. In a 2 + 2 design, this study asked if - holding dose level and dose d. constant - how simultaneous combination chemotherapy compared with purely sequential treatment, and - holding dose-level and combination or sequential use constant - how dose-d. influenced disease-free and overall survival in the post-operative adjuvant setting for node-pos. disease. Specifically, the study examined sequential doxorubicin, paclitaxel and cyclophosphamide compared with concurrent doxorubicin and cyclophosphamide followed by paclitaxel, and also dose-dense (every 2 wk administration) compared with conventional (every 3 wk administration) scheduling. The results, with long-term follow-up, confirm the predictions of the model. Not only is the shortened inter-treatment interval of chemotherapy better in terms of disease-free and overall survival, but it is less toxic as well. Combination chemotherapy (doxorubicin plus simultaneous cyclophosphamide) offers no advantage over sequential chemotherapy (doxorubicin followed later by cyclophosphamide) if dose level and dose d. are the same, except that combinations shorten overall treatment duration and are thus more convenient. These results

define a more effective, less toxic conceptual approach to the adjuvant chemotherapy of breast cancer, which should apply to all chemotherapy drugs given in the i.v. bolus format, even when biol. agents are added. Further development of the principles and methods established by CALGB 9741 are currently underway.

AN 2008:455730 HCAPLUS <<LOGINID::20090324>>

DN 149:23782

TI The concept of mathematically optimised dose-scheduling as applied to the adjuvant chemotherapy of primary breast cancer: theory and recent results

AU Norton, Larry

CS Memorial Sloan-Kettering Cancer Center, New York, NY, USA

SO EJC Supplements (2008), 6(2), 10-16
CODEN: ESJUB6

PB Elsevier Ltd.

DT Journal; General Review

LA English

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN

TI The safety of dose-dense doxorubicin and cyclophosphamide followed by paclitaxel with trastuzumab in HER-2/neu overexpressed/amplified breast cancer

AB Purpose Dose-dense (dd) doxorubicin and cyclophosphamide (AC) followed by paclitaxel (P) is superior to every 3-weekly AC followed by P. Given the demonstrated cardiac safety for trastuzumab (T) with conventionally scheduled AC followed by P, we tested the safety of dd AC followed by P with T. The primary end point was cardiac safety, and the secondary end points were time to recurrence and overall survival. Methods Patients with HER-2/neu immunohistochem. (IHC) 3+ or fluorescent in situ hybridization (FISH)-amplified breast cancer and baseline left ventricular ejection fraction (LVEF) of ≥ 55% were enrolled, regardless of tumor size or nodal status. Treatment consisted of AC (60/600 mg/m2) + 4 followed by P (175 mg/m2) + 4 every 2-weekly with pegfilgrastim (6 mg on day 2) + T + 1 yr. LVEF by radionuclide scan was obtained at baseline, at months 2, 6, 9, and 18. Results From Jan. 2005 to Nov. 2005, 70 patients were enrolled. The median age was 49 years (range, 27 to 72 years); median LVEF at baseline was 68% (range, 55% to 81%). At month 2 in 70 of 70 patients, the median LVEF was 67% (range, 58% to 79%); at month 6 in 67 of 70 patients, it was 66% (range, 52% to 75%); at month 9 in 68 of 70 patients, it was 65% (range, 50% to 75%); and at month 18 in 48 of 70 patients, it was 66% (range, 57% to 75%). As of Dec. 1, 2007, the median follow-up was 28 mo (range, 25 to 35 mo). One patient (1%) experienced congestive heart failure (CHF). There were no cardiac deaths. Conclusion Dose-dense AC followed by P/T followed by T is feasible and is not likely to increase the incidence of cardiac events compared to established regimens.

AN 2008:443293 HCAPLUS <<LOGINID::20090324>>

DN 149:24265

TI The safety of dose-dense doxorubicin and cyclophosphamide followed by paclitaxel with trastuzumab in HER-2/neu overexpressed/amplified breast cancer

AU Dang, Chau; Fornier, Monica; Sugarman, Steven; Troso-Sandoval, Tiffany; Lake, Diana; D'Andrea, Gabriella; Siedman, Andrew; Sklarin, Nancy; Dickler, Maura; Currie, Violante; Gilewski, Theresa; Moynahan, Mary Ellen; Drullinsky, Pamela; Robson, Mark; Wasserheit-Leiblich, Carolyn; Mills, Nancy; Steingart, Richard; Panageas, Katherine; Norton, Larry; Hudis, Clifford

CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

SO Journal of Clinical Oncology (2008), 26(8), 1216-1222
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Dose-dense therapy in the treatment of early-stage breast cancer: an overview of the data
AB A review. Breast cancer represents a significant public health burden with > 200,000 new cases diagnosed in the United States each year. Although a significant proportion of these new diagnoses represent early-stage disease, many of these women will eventually experience a distant relapse and ultimately die of complications of metastatic breast cancer. Consequently, innovations in adjuvant treatment strategies are critical as we strive to further optimize outcomes. One such innovation, the dose-dense approach, is intended to specifically optimize the administration of standard chemotherapy regimens. Specifically, models of tumor growth and response, based on the Norton-Simon hypothesis, were translated into regimens which aim to increase tumor cell kill by decreasing the time intervals between treatments. This strategy, fully evaluated with doxorubicin/cyclophosphamide and paclitaxel in Cancer and Leukemia Group B 9741, demonstrated significant benefits compared with conventionally scheduled adjuvant chemotherapy. Dose d. has since been applied to a number of other chemotherapy regimens and evaluated in clin. trials. An overview of the pivotal dose-dense trials will be reviewed herein.
AN 2008:162384 HCAPLUS <<LOGINID::20090324>>
DN 148:321612
TI Dose-dense therapy in the treatment of early-stage breast cancer: an overview of the data
AU McArthur, Heather L.; Hudis, Clifford A.
CS Breast Cancer Medicine Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
SO Clinical Breast Cancer (2007), 8(Suppl. 1), S6-S10
CODEN: CBCLB7; ISSN: 1526-8209
PB CIG Media Group, LP
DT Journal; General Review
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Taxanes as adjuvant therapy for breast cancer
AB A review. The report of the results of the first generation taxane trials has made evident that these drugs should play a key role in the adjuvant treatment of node-pos. operable breast cancer. Although direct comparisons among the different taxane regimens is still lacking, the American AC-paclitaxel dose-dense regimen, the TAC regimen, the French FEC-docetaxel and the Spanish FEC-paclitaxel regimens seem to offer the best results. The TC regimen (docetaxel-cyclophosphamide) is another option, particularly in patients at high risk for cardiac toxicity. Trastuzumab should now be part of the standard adjuvant treatment of HER-2/neu pos. breast cancer, probably administered in combination with a taxane regimen.
AN 2007:1287636 HCAPLUS <<LOGINID::20090324>>
DN 148:134743
TI Taxanes as adjuvant therapy for breast cancer
AU Martin, Miguel

CS Servicio de Oncologia Medica, Hospital Universitario San Carlos, Madrid, 28040, Spain
SO Women's Oncology Review (2006), 6(3-4), 137-144
CODEN: WOROAR; ISSN: 1473-3404
PB Taylor & Francis Ltd.
DT Journal; General Review
LA English
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Long-term assessment of cardiac function after dose-dense and -intense sequential doxorubicin (A), paclitaxel (T), and cyclophosphamide (C) as adjuvant therapy for high risk breast cancer
AB This study evaluated the incidence of late cardiotoxicity after dose-dense and -intense adjuvant sequential doxorubicin (A), paclitaxel (T), and cyclophosphamide (C) for breast cancer (BC) with ≥4 involved ipsilateral axillary lymph nodes. Patients were enrolled from 1994 to 2001 after definitive BC surgery if ≥4 axillary nodes were involved. Planned treatment was A 90 mg/m2 q 14 days + 3, T 250 mg/m2 q 14 days + 3, C 3 g/m2 q 14 days + 3 with filgrastim (G) support. Left ventricular ejection fraction (LVEF) was monitored using equilibrium radionuclide angiog. (ERNA) before the initiation of chemotherapy, and after three cycles of each chemotherapeutic agent. At a median follow-up of 7 years, we obtained ERNA scans on 32 patients to evaluate the long-term cardiotoxicity of this regimen. Eighty-five eligible patients enrolled on the treatment protocol. Clin. heart failure developed in one patient. Seven (8%) patients had LVEF <50% at the end of therapy. No cardiac-related deaths occurred. Thirty-two (46%) of 69 surviving patients have consented to late cardiac imaging. At a median follow-up of 7 years, the median absolute change in LVEF from baseline was -5.5%; [range (-8%) to (+36%)], and from the end of chemotherapy was -2.0%; [range (-25%) to (+16%)]. Four patients (12%) had a LVEF <50%; two of these four patients had an LVEF of <50% at the end of chemotherapy. Late development of asymptomatic decline in cardiac function may occur after dose-dense and -intense adjuvant therapy, but is uncommon.
AN 2007:875264 HCAPLUS <<LOGINID::20090324>>
DN 148:45224
TI Long-term assessment of cardiac function after dose-dense and -intense sequential doxorubicin (A), paclitaxel (T), and cyclophosphamide (C) as adjuvant therapy for high risk breast cancer
AU Abu-Khalaf, Maysa M.; Juneja, Vinni; Chung, Gina G.; DiGiovanna, Michael P.; Sipples, Rebecca; McGurk, Meghan; Zelterman, Daniel; Haffty, Bruce; Reiss, Michael; Wackers, Frans J.; Lee, Forrester A.; Burtness, Barbara A.
CS Department of Internal Medicine, Section of Medical Oncology, Yale Cancer Center, Yale University School of Medicine, New Haven, CT, 06520-8032, USA
SO Breast Cancer Research and Treatment (2007), 104(3), 341-349
CODEN: BCTRD6; ISSN: 0167-6806
PB Springer
DT Journal
LA English
RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Intensive dose-dense compared with high-dose adjuvant chemotherapy for high-risk operable breast cancer: southwest oncology group/intergroup study 9623
AB Southwest Oncol. Group (SWOG)/Intergroup study 9623 was undertaken to compare treatment with an anthracycline-based adjuvant chemotherapy

regimen followed by high-dose chemotherapy (HDC) with autologous hematopoietic progenitor cell support (AHPCS) with a modern dose-dense dose-escalated (nonstandard) regimen including both an anthracycline and a taxane. Participants in this phase III randomized study had operable breast cancer involving four or more axillary lymph nodes and had completed mastectomy or breast-conserving surgery. Patients were randomly assigned to receive four cycles of doxorubicin and cyclophosphamide followed by HDC with AHPCS or to receive sequential dose-dense and dose-escalated chemotherapy with doxorubicin, paclitaxel, and cyclophosphamide. The primary end point of this study was disease-free survival (DFS). Among 536 eligible patients, there was no significant difference between the two arms for DFS or overall survival (OS). Estimated five-year DFS was 80% (95% CI, 76% to 85%) for dose-dense therapy and 75% (95% CI, 69% to 80%) for transplantation. Estimated 5-yr OS was 88% (95% CI, 84% to 92%) for dose-dense therapy and 84% (95% CI, 79% to 88%) for transplantation. There is no evidence that transplantation was superior to dose-dense dose-escalated therapy. Transplantation was associated with an increase in toxicity and a possibly inferior outcome, although the hazard ratios were not significantly different from 1.

AN 2007:598772 HCAPLUS <<LOGINID::20090324>>
DN 147:203328
TI Intensive dose-dense compared with high-dose adjuvant chemotherapy for high-risk operable breast cancer: southwest oncology group/intergroup study 9623
AU Moore, Halle C. F.; Green, Stephanie J.; Gralow, Julie R.; Bearman, Scott I.; Lew, Danika; Barlow, William E.; Hudis, Clifford; Wolff, Antonio C.; Ingle, James N.; Chew, Helen K.; Elias, Anthony D.; Livingston, Robert B.; Martino, Silvana
CS Cleveland Clinic Foundation, Cleveland, OH, USA
SO Journal of Clinical Oncology (2007), 25(13), 1677-1682
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Concepts and clinical trials of dose-dense chemotherapy for breast cancer
AB This article will review the strategy of dose-dense administration of chemotherapy for breast cancer. Increased dose d. is achieved by reducing the interval between each dose of chemotherapy. The cumulative drug dose remains constant, but the same amount of drug is administered over a shorter period. Math. models of tumor growth have provided the basis for the clin. application of dose-dense chemotherapy. The Norton-Simon model suggests that increasing the dose d. of chemotherapy will increase efficacy by minimizing the opportunity for regrowth of tumor cells between cycles of chemotherapy. Intergroup trial 9741, coordinated by the Cancer and Leukemia Group B (CALGB), tested the 2 hypotheses that dose-dense and sequential administration of chemotherapy regimens incorporating doxorubicin, cyclophosphamide, and paclitaxel would improve disease-free survival and overall survival. A statistically significant 4-yr disease-free survival advantage was detected for the 2 dose-dense regimens compared with the regimens administered every 3 wk. The math. concepts and previous clin. trials of dose d. that contributed to the design of CALGB 9741 will be reviewed. The strengths and limitations of CALGB 9741 will then be discussed before the presentation of future directions of research and recommendations for

clin. practice today.
AN 2006:84758 HCAPLUS <<LOGINID::20090324>>
DN 145:20182
TI Concepts and clinical trials of dose-dense chemotherapy for breast cancer
AU Orzano, Jennifer A.; Swain, Sandra M.
CS Cancer Therapeutics Branch, Center for Cancer Research, Department of Health & Human Services, National Cancer Institute, Bethesda, MD, USA
SO Clinical Breast Cancer (2005), 6(5), 402-411
CODEN: CBCLB7; ISSN: 1526-8209
PB CIG Media Group, LP
DT Journal; General Review
LA English
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Efficacy of pegfilgrastim and darbepoetin alfa as hemotopoietic support for dose-dense every-2-week adjuvant breast cancer chemotherapy
AB Purpose Dose-dense, every-2-wk adjuvant chemotherapy using doxorubicin/cyclophosphamide (AC; 60/600 mg/m2 every 2 wk + four cycles) followed by paclitaxel (175 mg/m2 every 2 wk + four cycles), requiring filgrastim on days 3 through 10 of each cycle has been shown to improve survival compared with every-3-wk treatment schedules but is associated with greater risk of RBC transfusion (13%). The role of long-acting hematopoietic growth factors in facilitating every-2-wk chemotherapy and minimizing hematol. toxicity has not been established. Patients and Methods Women with stage I to III breast cancer received dose-dense AC → paclitaxel as neoadjuvant or adjuvant chemotherapy. Patients received pegfilgrastim 6 mg s.c. (SQ) on day 2 of each cycle. Darbepoetin alfa was initiated at 200 μg SQ every 2 wk for Hb ≤ 12 g/dL, and administered thereafter, according to a preplanned algorithm. The primary end points were to evaluate the percentage of patients with febrile neutropenia and the percentage of patients requiring RBC transfusion. Results Among 135 women treated on this single arm study, there were two cases of febrile neutropenia (incidence 1.5%). No patients received RBC transfusion. Darbepoetin alfa therapy was initiated in 92% of patients. The modest leukocytosis seen during paclitaxel cycles was attributable, in part, to corticosteroid premedication. Other toxicity and dose-delivery were similar to dose-dense AC → paclitaxel in Cancer and Leukemia Group B 9741. Conclusion Pegfilgrastim and darbepoetin alfa are effective and safe in facilitating every-2-wk AC → paclitaxel, minimizing rates of febrile neutropenia and RBC transfusion.
AN 2005:1312471 HCAPLUS <<LOGINID::20090324>>
DN 144:304669
TI Efficacy of pegfilgrastim and darbepoetin alfa as hemotopoietic support for dose-dense every-2-week adjuvant breast cancer chemotherapy
AU Burstein, Harold J.; Parker, Leroy M.; Keshaviah, Aparna; Doherty, Jennifer; Partridge, Ann H.; Schapira, Lidia; Ryan, Paula D.; Younger, Jerry; Harris, Lyndsay N.; Moy, Beverly; Come, Steven E.; Schumer, Susan T.; Bunnell, Craig A.; Haldoupis, Margaret; Gelman, Rebecca; Winer, Eric P.
CS Dana-Farber Cancer Institute, Boston, MA, USA
SO Journal of Clinical Oncology (2005), 23(33), 8340-8347
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Five-year update of an expanded phase II study of dose-dense and -intense doxorubicin, paclitaxel and cyclophosphamide (ATC) in high-risk breast cancer
AB This study evaluated the safety and efficacy of dose-dense and -intense sequential doxorubicin (A), paclitaxel (T) and cyclophosphamide (C) as adjuvant therapy for breast cancer (BC) with ≥4 ipsilateral axillary lymph nodes. Patients were recruited after BC surgery if ≥4 axillary nodes were involved by metastatic cancer. Planned treatment was A 90 mg/m2 three times every 14 days (q14d + 3), T 250 mg/m2 q14d + 3 and C 3 g/m2 q14d + 3 combined with filgrastim support. The study enrolled 85 eligible patients. The median number of lymph nodes involved was 9. Mean dose intensity was >94% of planned for each drug. Common grade 3 toxicities included nausea and/or vomiting (24%), mucositis (18%), neuropathy (16%), palmar-plantar erythrodysesthesia (12%), myalgia (6%) and arthralgia (6%). Grade 3/4 neutropenia occurred in 77 (91%) patients, and 32 (38%) patients had neutropenic fever. One patient developed acute leukemia. Sixty-nine (81%) patients are alive, and 59 (69%) patients are alive and free of distant disease at a median follow-up of 5 years. ATC is a feasible regimen for adjuvant therapy of high-risk BC, with a relatively low rate of relapse at the 5-yr follow up.
AN 2005:1311866 HCAPLUS <<LOGINID::20090324>>
DN 144:343146
TI Five-year update of an expanded phase II study of dose-dense and -intense doxorubicin, paclitaxel and cyclophosphamide (ATC) in high-risk breast cancer
AU Abu-Khalaf, Maysa M.; Windsor, Stephen; Ebisu, Keita; Salikooti, Saritha; Ananthanarayanan, Gowri; Chung, Gina G.; DiGiovanna, Michael P.; Haffty, Bruce G.; Abrams, Martin; Farber, Leonard R.; Hsu, Arlene D.; Reiss, Michael; Zelterman, Daniel; Burtness, Barbara A.
CS Jersey Shore University Medical Center, Neptune, NJ, USA
SO Oncology (2005), 69(5), 372-383
CODEN: ONCOBS; ISSN: 0030-2414
PB S. Karger AG
DT Journal
LA English
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of intergroup trial C9741/cancer and leukemia group B trial 9741. [Erratum to document cited in CA142:273450]
AB The corrected version of Table 6 is given.
AN 2005:279234 HCAPLUS <<LOGINID::20090324>>
DN 142:309436
TI Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of intergroup trial C9741/cancer and leukemia group B trial 9741. [Erratum to document cited in CA142:273450]
AU Citron, Marc L.; Berry, Donald A.; Cirrincione, Constance; Hudis, Clifford; Winer, Eric P.; Gradishar, William J.; Davidson, Nancy E.; Martino, Silvana; Livingston, Robert; Ingle, James N.; Perez, Edith A.; Carpenter, John; Jurd, David; Solland, James F.; Smith, Barbara L.;

Sartor, Carolyn I.; Leung, Eleanor H.; Abrams, Jeffrey; Schilsky, Richard L.; Muss, Hyman B.; Norton, Larry
CS ProHEALTH Care Associates, LLP, Lake Success, NY, USA
SO Journal of Clinical Oncology (2003), 21(11), 2226
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English

L6 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Dose-dense & sequential adjuvant cancer chemotherapy
AB Breast cancer is treated by (a) administering to a patient in a first plurality of chemotherapy cycles a therapeutically-effective and well-tolerated amount of doxorubicin in a dose-dense protocol; (b) subsequently administering to the patient in a second plurality of chemotherapy cycles a therapeutically-effective and well-tolerated amount of a taxane chemotherapy agent, for example paclitaxel, in a dose-dense protocol; and (c) subsequently administering to the patient in a third plurality of chemotherapy cycles a therapeutically-effective and well-tolerated amount of cyclophosphamide in a dose-dense protocol. Preferably, the dose dense interval between treatments is about 14 days. The number of cycles in each plurality of chemotherapy cycles is suitably 3 or more, preferably 4. Suitable well-tolerated treatment levels are 60 mg/m 2 of doxorubicin, 175 mg/ 2 of paclitaxel, and 600 mg/ 2 of cyclophosphamide. A therapeutically effective amount of G-CSF may also be administered during the intervals between treatments in one or more of the chemotherapy cycles.
AN 2004:995765 HCAPLUS <<LOGINID::20090324>>
DN 141:406045
TI Dose-dense & sequential adjuvant cancer chemotherapy
IN Norton, Larry
PA USA
SO U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20040229826	A1	20041118	US 2003-735180	20031212
PRAI	US 2002-432840P	P	20021212		

L6 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of intergroup trial C9741/cancer and leukemia group B trial 9741
AB Using a 2 + 2 factorial design, we studied the adjuvant chemotherapy of women with axillary node-pos. breast cancer to compare sequential doxorubicin (A), paclitaxel (T), and cyclophosphamide (C) with concurrent doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) for disease-free (DFS) and overall survival (OS); to determine whether the dose d. of the agents improves DFS and OS; and to compare toxicities. A total of 2,005 female patients were randomly assigned to receive one of the following regimens: (I) sequential A + 4 (doses) → T + 4 → C + 4 with doses every 3 wk, (II) sequential A + 4 → T + 4 → C + 4 every 2 wk with filgrastim, (III) concurrent AC + 4 → T + 4 every 3 wk, or (IV) concurrent AC + 4 → T + 4 every 2 wk with filgrastim.

A protocol-specified anal. was performed at a median follow-up of 36 mo: 315 patients had experienced relapse or died, compared with 515 expected treatment failures. Dose-dense treatment improved the primary end point, DFS (risk ratio [RR] = 0.74; P = .010), and OS (RR = 0.69; P = .013). Four-year DFS was 82% for the dose-dense regimens and 75% for the others. There was no difference in either DFS or OS between the concurrent and sequential schedules. There was no interaction between d. and sequence. Severe neutropenia was less frequent in patients who received the dose-dense regimens. Dose d. improves clin. outcomes significantly, despite the lower than expected number of events at this time. Sequential chemotherapy is as effective as concurrent chemotherapy.

AN 2004:934715 HCAPLUS <<LOGINID::20090324>>
DN 142:273450
TI Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of intergroup trial C9741/cancer and leukemia group B trial 9741
AU Citron, Marc L.; Berry, Donald A.; Cirrincione, Constance; Hudis, Clifford; Winer, Eric P.; Gradishar, William J.; Davidson, Nancy E.; Martino, Silvana; Livingston, Robert; Ingle, James N.; Perez, Edith A.; Carpenter, John; Hurd, David; Holland, James F.; Smith, Barbara L.; Sartor, Carolyn I.; Leung, Eleanor H.; Abrams, Jeffrey; Schilsky, Richard L.; Muss, Hyman B.; Norton, Larry
CS ProHEALTH Care Associates, LLP, Lake Success, NY, USA
SO Journal of Clinical Oncology (2003), 21(8), 1431-1439
CODEN: JCONDN; ISSN: 0732-183X
PB American Society of Clinical Oncology
DT Journal
LA English
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Dose-dense treatment prolongs disease-free survival of women with node positive breast cancer
AB A review and discussion. The impact of dose d. and drug sequence (concurrent vs. sequential) in women with axillary node-pos. primary breast cancer was assessed. Breast cancer is the second leading cause of cancer mortality in women. The prognosis for patients with extensive axillary lymph nodes involvement is poor. Important trial demonstrated that shortening the time interval between each chemotherapy cycle while maintaining the same dose size resulted in a significant improvement in disease-free and overall survival in patients with node-pos. breast cancer without increase in toxicity. A dose-dense treatment regimen significantly improved clin. outcomes in women with axillary node-pos. primary breast cancer. Concurrent chemotherapy is proved to be as effective as sequential chemotherapy.

AN 2003:705588 HCAPLUS <<LOGINID::20090324>>
DN 140:263316
TI Dose-dense treatment prolongs disease-free survival of women with node positive breast cancer
AU Dang, Chau; Seidman, Andrew D.
CS Breast Cancer Medicine Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
SO Cancer Treatment Reviews (2003), 29(5), 453-456
CODEN: CTREDJ; ISSN: 0305-7372
PB Elsevier Science Ltd.
DT Journal; General Review
LA English

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI A Pilot Study of Dose Intense Doxorubicin and Cyclophosphamide Followed by Infusional Paclitaxel in High-Risk Primary Breast Cancer
AB We conducted a pilot study of dose dense doxorubicin and cyclophosphamide (AC) combination chemotherapy followed by infusional paclitaxel (T) in primary breast cancer to determine its safety and feasibility. Twenty-two subjects (10 with stage II and ≥4 pos. lymph nodes, and 12 with stage III disease) were treated with AC (A 60 mg/m2 and C 2000 mg/m2) with filgrastim every 14 days for three cycles followed by infusional paclitaxel (140 mg/m2 over 96 h) every 14 days for three cycles. Mean overall cycle length was 15.3 days and mean duration of therapy was 92 days. Dose redns. of C or T were required in 7/132 (5.3%) cycles for mucositis, diarrhea, or failure to recover platelets by day 15. Ninety-five percent of subjects had grade 4 neutropenia and 1 subject had a platelet nadir of <20,000. Actual delivered dose intensity (DI) over six cycles was: A 27 mg/m2 per wk; C 892 mg/m2 per wk; T 64 mg/m2 per wk (90.6, 89.2, and 91.4% of planned DI, resp.). Average total dose administered was: A 180 mg/m2; C 5880 mg/m2; T 403 mg/m2 (100, 98, and 96% of planned total doses, resp.). Clin. response rate in 10 subjects receiving neoadjuvant therapy was 100% (4 complete response, 6 partial response). Four subjects had a pathol. complete response (three subjects without evidence of malignancy and one subject with ductal carcinoma in situ.). Administration of dose dense AC followed by infusional paclitaxel in 14-day cycles is feasible and this regimen is active in breast cancer.
AN 2003:665006 HCAPLUS <<LOGINID::20090324>>
DN 140:174554
TI A Pilot Study of Dose Intense Doxorubicin and Cyclophosphamide Followed by Infusional Paclitaxel in High-Risk Primary Breast Cancer
AU Zujewski, Jo Anne; Eng-Wong, Jennifer; O'Shaughnessy, Joyce; Venzon, David; Chow, Catherine; Danforth, David; Kohler, David R.; Cusack, Georgia; Riseberg, David; Cowan, Kenneth H.
CS National Cancer Institute, National Institutes of Health, Bethesda, MD, USA
SO Breast Cancer Research and Treatment (2003), 81(1), 41-51
CODEN: BCTRD6; ISSN: 0167-6806
PB Kluwer Academic Publishers
DT Journal
LA English
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Doxorubicin followed by sequential paclitaxel and cyclophosphamide versus concurrent paclitaxel and cyclophosphamide: 5-year results of a Phase II randomized trial of adjuvant dose-dense chemotherapy for women with node-positive breast carcinoma
AB We conducted a randomized Phase II trial to directly compare toxicity, feasibility, and delivered dose intensities of two adjuvant dose-intensive regimens containing doxorubicin, paclitaxel, and cyclophosphamide for patients with node-pos. breast carcinoma. Forty-two patients with resected breast carcinoma involving one or more ipsilateral axillary lymph nodes, were randomized to receive two different schedules of adjuvant chemotherapy using 14-day dosing intervals: either (a) three cycles of doxorubicin 80 mg/m2 as i.v. bolus followed sequentially by three cycles of paclitaxel 200 mg/m2 as a 24-h infusion and then by three cycles of cyclophosphamide 3.0 g/m2 as a 1-h infusion (arm A); or (b) the same schedule of doxorubicin followed by three cycles of concurrent cyclophosphamide and

paclitaxel at the same doses (arm B). All cycles were supported by granulocyte colony-stimulating factor administration. Forty-one patients were assessable for toxicity and feasibility; 37 (90%) completed all planned chemotherapy. There was no treatment-related mortality; however, increased toxicity was observed on arm B compared with arm A, manifested by an increase in hospitalization for toxicity, mainly neutropenic fever, and an increased incidence of transfusion of packed RBCs transfusions for anemia. The mean delivered dose intensities for paclitaxel and cyclophosphamide were significantly greater for arm A compared with arm B (P = .01 and P = .05, resp.). There is no long-term, treatment-related toxicity, and no cases of acute myelogenous leukemia or myelodysplastic syndrome have been observed Dose-dense sequential single-agent chemotherapy is more feasible than doxorubicin with subsequent concurrent paclitaxel and cyclophosphamide.

AN 2002:51000 HCAPLUS <<LOGINID::20090324>>

DN 136:256842

TI Doxorubicin followed by sequential paclitaxel and cyclophosphamide versus concurrent paclitaxel and cyclophosphamide: 5-year results of a Phase II randomized trial of adjuvant dose-dense chemotherapy for women with node-positive breast carcinoma

AU Fornier, Monica N.; Seidman, Andrew D.; Theodoulou, Maria; Moynahan, Mary Ellen; Currie, Violante; Moasser, Mark; Sklarin, Nancy; Gilewski, Theresa; D'Andrea, Gabriella; Salvaggio, Rori; Panageas, Kathy S.; Norton, Larry; Hudis, Clifford

CS Breast Cancer Medicine Service, Weill Medical College of Cornell University, New York, NY, 10021, USA

SO Clinical Cancer Research (2001), 7(12), 3934-3941
CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Sequential dose-dense doxorubicin, paclitaxel, and cyclophosphamide for resectable high-risk breast cancer: feasibility and efficacy

AB Dose-dense chemotherapy is predicted to be a superior treatment plan. Therefore, we studied dose-dense doxorubicin, paclitaxel, and cyclophosphamide (A → T → C) as adjuvant therapy. Patients with resected breast cancer involving four or more ipsilateral axillary lymph nodes were treated with nine cycles of chemotherapy, using 14-day intertreatment intervals. Doses were as follows: doxorubicin 90 mg/m2 + 3, then paclitaxel 250 mg/m2/24 h + 3, and then cyclophosphamide 3.0 g/m2 + 3; all doses were given with s.c. injections of 5 μg/kg granulocyte colony-stimulating factor on days 3 through 10. Amenorrheic patients with hormone receptor-pos. tumors received tamoxifen 20 mg/day for 5 yr. Patients treated with breast conservation, those with 10 or more pos. nodes, and those with tumors larger than 5 cm received radiotherapy. Between Mar. 1993 and June 1994, we enrolled 42 patients. The median age was 46 yr (range, 29 to 63 yr), the median number of pos. lymph nodes was eight (range, four to 25), and the median tumor size was 3.0 cm (range, 0 to 11.0 cm). The median intertreatment interval was 14 days (range, 13 to 36 days), and the median delivered dose-intensity exceeded 92% of the planned dose-intensity for all three drugs. Hospital admission was required for 29 patients (69%), and 28 patients (67%) required blood product transfusion. No treatment-related deaths or cardiac toxicities occurred. Doxorubicin was dose-reduced in four patients (10%) and paclitaxel was reduced in eight (20%). At a median follow-up from surgery of 48 mo

(range, 3 to 57 mo), nine patients (19%) had relapsed, the actuarial disease-free survival rate was 78% (95% confidence interval, 66% to 92%), and four patients (10%) had died of metastatic disease. Dose-dense sequential adjuvant chemotherapy with doxorubicin, paclitaxel, and cyclophosphamide (A → T → C) is feasible and promising. Several ongoing phase III trials are evaluating this approach.

AN 1999:50879 HCAPLUS <<LOGINID::20090324>>

DN 130:232080

TI Sequential dose-dense doxorubicin, paclitaxel, and cyclophosphamide for resectable high-risk breast cancer: feasibility and efficacy

AU Hudis, C.; Seidman, A.; Baselga, J.; Raptis, G.; Lebwohl, D.; Gilewski, T.; Moynahan, M.; Sklarin, N.; Fennelly, D.; Crown, J. P. A.; Surbone, A.; Uhlenhopp, M.; Riedel, E.; Yao, T. J.; Norton, L.

CS Breast and Gynecologic Cancer Medicine Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10024, USA

SO Journal of Clinical Oncology (1999), 17(1), 93-100
CODEN: JCONDN; ISSN: 0732-183X

PB Lippincott Williams & Wilkins

DT Journal

LA English

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT